IN THE CLAIMS

36. (Amended) An isolated nucleic acid having a nucleotide sequence encoding an amino acid sequence depicted in Figure 4, SEQ ID NO: 2, which is flanked by a heterologous sequence.

45. (Amended) An isolated nucleic acid having a nucleotide sequence encoding an amino acid sequence comprising amino acids 1-45 of Figure 4, SEQ ID NO:2.

REMARKS

I. Status of the Claims

Claims 27-61 are pending. Claims 27-44 have been allowed. Claim 36 has been amended to insert a comma after the term "Figure 4" in the interest of clarity. Claim 45 has been amended to clarify that the sequence is a "nucleotide" sequence.

II. Response to Examiner's Comments in Advisory Action

In the Advisory Action, the Examiner has maintained the rejection of claims 45-49 on the grounds that the claims are not enabled by the specification. The Examiner states that the "claims do not disclose the 'critical technical feature of the invention'." (Advisory Action, page 1, paragraph 6)

This rejection is traversed, and reconsideration is respectfully requested.

Applicants respectfully draw the attention of the Examiner to the MPEP § 2164.08(c) which states (emphasis added):

> An enablement rejection based on the grounds that a disclosed critical limitation is missing from a claim should be made only when the language of the specification makes it clear that the limitation is critical for the invention to function as intended. Broad language in the disclosure, including the abstract, omitting an allegedly critical feature, tends to rebut the argument of criticality.

In light of the forgoing statements, the Examiner's grounds for rejecting claims 45-49 are not appropriate.[1] The present claims omit no critical limitation. Claims 45-49 recite the novel feature of the invention in terms of structure, which is the novel amino acid sequence 1-45 of SEQ ID NO:2. The inventive feature has well known utility, e.g., for generating antibodies, but the claims are directed to the products, not any particular function as the Examiner appears to be suggesting in the first full paragraph on page 4 of paper no.15. Furthermore, the invention also encompasses methods for identifying hERβ-interactive compounds, including agonists, antagonists, and co-activators.

The present specification discloses the novel amino acid sequence 1-45. This disclosure is all that is necessary to enable claims 45-49.

Furthermore, one skilled in the art would not require undue experimentation to practice the invention as asserted by the Examiner. "Enablement is not precluded by the necessity for some experimentation such as routine screening.

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[1] If the Examiner founded this rejection on the basis of some other authority, applicants request that the Examiner identify this authority.

However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue' not experimentation." *In re Wands*, 858 F. 2d 736 (Fed Cir. 1988). The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable guidance with respect to the direction in which the experimentation should proceed. *In re Wands*, 858 F.2d 736 quoting *In re Jackson*, 217 USPQ at 807.

Those skilled in the art, having at hand the novel amino acid sequence 1-45 (SEQ ID NO: 2), would have been able to practice the invention at the time the present application was filed using conventional techniques in molecular biology, microbiology, and recombinant DNA. The specific references recited from page 14, line 17 to page 5, line 4 of the instant specification disclose conventional techniques to be utilized in practicing the invention at the time the application was filed. Therefore, the specification provides all reasonable guidance necessary to practice the invention.

III. Withdrawal of Claims 50-61

The Examiner has withdrawn claims 50-61 from consideration contending that they are drawn to the invention Group III, and are distinct from the elected invention of Group I for the reason of record, see paper 4, dated 9/3/98.

This withdrawal is respectfully traversed, and rejoinder is requested.

Claims 50-61 are directed to a method of using a cell that expresses a novel hERβ as a result of comprising a DNA vector of the invention. To the extent that the nucleic acid, vector and cell line compositions of matter are novel and nonobvious, the methods of using these composition in a biotechnological process of screening for ligands is also novel and nonobvious. 35 U.S.C. §103(b)(1)(A).[2] Thus, claims 50-61 are directed to a method of using a product produced by a process of genetically altering an organism to express an exogenous nucleotide sequence. 35 U.S.C. §103(b)(3)(A) and (C).

Furthermore, "if applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims which depend from or otherwise include all the limitations of the allowable product claim will be rejoined" (MPEP 821.04). Applicant provisionally elected claims 1-16 (new claims 27-44) directed to the product in the amendment filed October 5, 1998. Product claims 27-44 were subsequently found allowable in the Final Office Action mailed June 6, 2001. Withdrawn process claims 50-61 contain all the limitations of the allowable product claims. Therefore, rejoinder is required in this case.

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[2]The composition of matter and process were owned by the same person or subject to an obligation of assignment to the same person at the time they were invented. 35 U.S.C. §103(b)(1)(B).

IV. Rejection under 35 U.S.C § 112, first paragraph

Claims 45-49 have been rejected under 35 U.S.C § 112, first paragraph as non-enabled. The Examiner contends that the specification does not reasonably provide enablement for nucleic acids comprising a sequence encoding an amino acid sequence consisting of amino acids 1-45 of SEQ ID NO:2 and vectors encoding the fusion protein and cells comprising the fusion protein. Specifically, the Examiner asserts that the specification fails to provide sufficient information on the function of the fragment encoding amino acids 1-45 of SEQ ID NO:2, such as definitive structural features and their relationship to function.

This rejection is respectfully traversed and reconsideration is requested.

Claims 45-49 recite structure, not a function as the Examiner appears to be suggesting. Perhaps the Examiner implies that the claimed subject matter is not useful. The polypeptides encoded by the claimed nucleic acids have utility, e.g., for generating antibodies. One advantage of such antibodies would be their ability to specifically bond to the novel estrogen β receptor of the invention. The specification at page 22, lines 13 to page 24, line 3 describes making antibodies, and beginning on page 24, line 5 describes the application of using such antibodies to identify compounds that interact with hERβ. Furthermore, the invention also encompasses methods for identifying hERβ-interactive compounds, including agonists, antagonists, and co-activators, which identification process benefits from testing on a hERβ with the claimed N-terminal sequence (see page 35, lines 8-10).

Also, with respect to claims 45-49, the Examiner further contends that the instant disclosure of a single distinct polypeptide, and nucleic acid encoding said polypeptide, does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera including full-length, truncated, mutated, variant and fusion proteins encoded by the disclosed nucleic acids.

Applicants respectfully traverse this contention. Given any useful polypeptide, and the nucleic acid encoding it, one of ordinary skill in the art is enabled to generate numerous constructs comprising such polypeptide, including full length estrogen β receptors, fusion proteins, or polypeptide fragments. The claimed protein is, in this respect, no different from any other patentable product, such as a chemical (which might find itself in any number of compositions and formulations, whether or not envisioned by the inventor of the chemical), or an electronic transistor (which might be included in a hand-held radio, an automobile, or an interplanetary space vehicle, whether or not envisioned by the inventor). This claim provides the inventors with the exclusive right to what is properly theirs: an isolated nucleic acid having a nucleotide sequence encoding an amino acid sequence comprising amino acids 1-45 of Figure 4 (SEQ ID NO: 2), whatever other components may be present.

The Examiner properly should not dispute that the 1-45 sequence is useful. At the time this invention was made, the ordinary skilled artisan, given any polypeptide and any nucleic acid encoding it, could engineer a multitude of constructs comprising the polypeptide. To argue otherwise ignores the abundant literature

describing a plethora of fusion products, as well as the plethora of commercial vectors that permit expression of polypeptide fusion proteins. Perhaps foremost among them the yeast two-hybrid system. Enumeration of all these systems at this point in time necessitates unending pages and exhibits. Applicants believe the Examiner is well aware of the literature and that such products are commercially available. Indeed, the Court of Appeals for the Federal Circuit, which Court's precedent binds the PTO, recognized that generating fusion constructs was state of the art in 1976: "translation of a ribosmal DNA -- which is not normally translated -- in a fusion protein with β galactosidase established with a reasonable expectation of success that one could express any protein this way." *See In re O'Farrell*, 7 U.S.P.Q.2d 1673, 1678-9 (Fed. Cir. 1988) (discussing a 1976 prior art reference) (emphasis added).

However, some additional fusion protein systems (besides full length β estrogen receptor, the 1-45 fragment, and an O'Farrell-type β galactosidase fusion) are noted in the references cited in the Amendment Under 37 C.F.R.§1.116, filed September 5, 2001, which is incorporated herein by reference in its entirety.

In light of the foregoing remarks, Applicants respectfully request withdrawal of this rejection.

In view of the above amendment and remarks, all of the pending claims are now believed to be in condition for allowance. Allowance of all the pending claims is earnestly solicited.

Respectfully submitted,

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Docket No: 0646/0D205

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Ramesh A. Bhat

Serial No.: 08/906,365 Art Unit: 1646

Filed: August 5, 1997 Examiner: N. Basi

For: Novel Human Estrogen Receptor-Beta

MARKUP TO SUPPLEMENTAL AMENDMENT

Hon. Commissioner of
Patents and Trademarks
Washington, DC 20231

October 25, 2001

Sir:

IN THE CLAIMS

36. An isolated nucleic acid having a sequence encoding an amino acid sequence depicted in Figure 4, SEQ ID NO:2, which is flanked by a heterologous sequence.

45. An isolated nucleic acid having a nucleotide sequence encoding an amino acid sequence [consisting of] comprising amino acids 1-45 of Figure 4, SEQ ID NO:2.

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